adaptive control, predictive control, constraints,
functional electrical stimulation, muscle, type I diabetes

Clara IONESCU*, Robin DE KEYSER

SOME CHALLENGING FEEDBACK-CONTROL APPLICATIONS IN BIOMEDICAL SYSTEMS

Natural biological control involves the normal functioning of the living organism (i.e. human body) to regulate its parameters such that the vital functions are kept within the normal operating range. When this natural control fails, the biological feedback (thus a closed loop system) is unstable and/or operates under non-optimal conditions of the vital capacity of the subject. In this context, ensuring surviving capacity of the subject implies to artificially control the vital functions presenting the functional failure. Nowadays technology enables development of artificial closed loop devices to correct and provide the normal functions of the organism, replacing thus the damaged/non-optimal parts or helping in recovering their natural properties (rehabilitation techniques). Two of the most en-vogue applications of artificial control will exemplify the importance and the posed challenges: - a *neuroprothesis* device to control paralyzed skeletal muscles; this enables rehabilitation of drop-foot or hand-grasp movements with paretic or paralyzed skeletal muscles by use of a self-adaptive (auto-tuning) control strategy; - and an *artificial pancreas* for diabetes type I patients; the blood glucose control in diabetic patients type I is made by use of an *in-house* developed model-based predictive control algorithm in which input (insulin rate) and output (glucose level) are constrained.

1. INTRODUCTION

1.1. REGULATION AND CONTROL IN PHYSIOLOGICAL SYSTEMS

The field of biomedical engineering is relatively young compared to the field of control and automation and is one of the most spectacular in terms of interdisciplinarity. It takes knowledge of biology, physiology, medical, engineering sciences and so much more to make one ready to explore the *terra nova* of nowadays science. It has been known for many years that the biological world contains many feedback mechanisms and structures, and therefore it was appealing for control engineers as an un-explored application field [9, 13]. Nowadays, the result is a manifold of applications of classic and advanced control strategies to biological systems, as a clearly defined ongoing research topic. Scientists applied their knowledge of mathematical modelling and systems analysis to various areas of bio-medicine and identified those physiological functions not yet described in mathematical terms. This knowledge-information created a *playground* to control engineers but only nowadays, thanks to developments in instrumentation, their ideas and work has been meaningful, offering practical solutions to modern control problems in biomedicine.

* Ghent University, Faculty of Engineering, EeSA Department of Electrical energy, Systems and Automation, Technologiepark 913, B9052 Gent, Belgium, clara@autoctrl.UGent.be

The overall beneficial impact of controlled biological systems on contemporary societies is a strong motivation to pursue in this challenging field.

Today's control applications in the field of biomedical engineering can be categorised in four main groups: - cardio- and hemo- dynamics control; - artificial limbs, gait analysis; - artificial ventilation; - drug delivery systems. The contribution will present and analyse results from two of the four categories: locomotion control and drug delivery control.

1.2. GOAL OF THIS CONTRIBUTION

The goal of this contribution is to give a practical-oriented overview upon 2 of the *hot-spots* in control applications within biomedical engineering area. As mentioned earlier, they tackle locomotion control and drug delivery control. Such systems are usually time-variant, nonlinear and pose constraints. They are highly dependent on developments in instrumentation and have a significant impact in the patient's life and consequently in the society. Performance analysis is provided both from the control engineering as well as from the physiological standpoint, in terms of real-life implementation.

The first example deals with a paralyzed skeletal muscle control via functional electrical stimulation and is the subject of the second section of this paper. An autotuning technique – no model of the system to be controlled is required – is presented along with its simulation results. Direct adaptive control (DIRAC) strategy is implemented in a discrete manner to simulate real-life practical implementation aspects. A nominal linearized model of the skeletal muscle is used for simulation purposes.

In a third section, the next example makes a comparison in terms of complexity between the use of a linearized model and a nonlinear model of a type I diabetic patient, in a predictive control scheme. An *in-house* Extended Predictive Self-Adaptive Control (EPSAC) algorithm is used to perform tests. Real-life constraints are imposed and results are provided by simulation.

Results are discussed by means of implementation and performance analysis in a fourth section and the main ideas of feedback control loops within biomedical applications are stressed.

2. APPLICATION I: PARALYZED SKELETAL MUSCLE CONTROL

Artificial control of paralyzed or paretic muscles (i.e. neuroprothesis) became a challenging field and lately an important research topic, stimulated by the advances in technology and instrumentation. One of the latest research outcome in this topic is the use of functional electrical stimulation (FES) to produce force in a skeletal muscle control loop [14]. A DIRAC (DIRect Adaptive Control) control strategy makes the objective of this feedback-controlled application study. The DIRAC algorithm is both an auto-tuning as well as an adaptation method for the controller parameters. Since paralyzed or paretic muscles are time-varying systems, an adaptive/auto-tuning method is therefore justified. A simple simulation on a muscle model adapted from literature is performed and the controller performance for reference tracking is depicted. A comparison between a classical control approach (PI and PID) and a DIRAC-PI controller is given in [10], including some implementation aspects of a model without time-delay considerations.

2.1. A SIMPLIFIED MUSCLE MODEL

A linear model capturing the properties of a muscle under isometric conditions can be represented by a 2nd order transfer function [6]:

$$M(s) = \frac{450e^{-0.005s}}{(s+5)(s+20)} \qquad (1)$$

The parameters (450, 5, 20, 0.005) are a set of *nominal* parameters and their value can change (considerably) from person-to-person. These parameters depend on the physical condition of the muscle, age etc. In case of a paralyzed muscle, important variations are observed during the rehabilitation period. The time delay occurring between the nervous activation and calcium release in muscle to obtain contraction has been taken into account (from *control engineering* standpoint, it is of no importance, because this time-delay is very small compared to the system time constants).

The input to such a model is a stimulus occurring with a certain frequency and the output is the force given by the contraction of the muscle, as in Figure 1. The input frequency is limited between 5Hz – 50Hz (the frequencies for which the static characteristic is linear and corresponds to equation (1)). From a mathematical standpoint, the response *y(t)* of the process M(s) to an input $u(t)$ (= frequency F) is the effect of a series of impulses with period T (= *1/F*) applied as input. A simple experiment (unit impulses) depicted by Figure 2 shows the output of the process corresponding to (1) and, having the time constants: 1/20=50 ms and 1/5=200 ms, a total open-loop settling time of about 1 second.

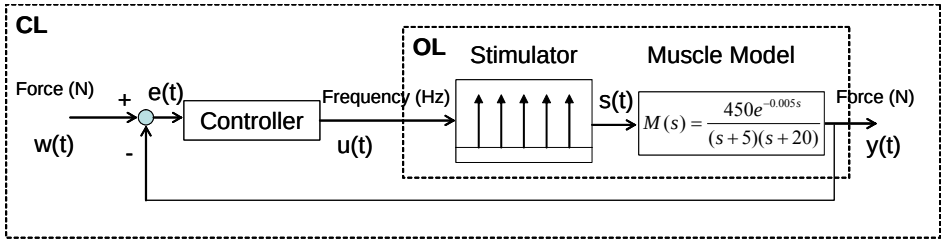

Fig. 1. Block scheme of muscle model simulation (open loop OL and closed loop CL configuration)

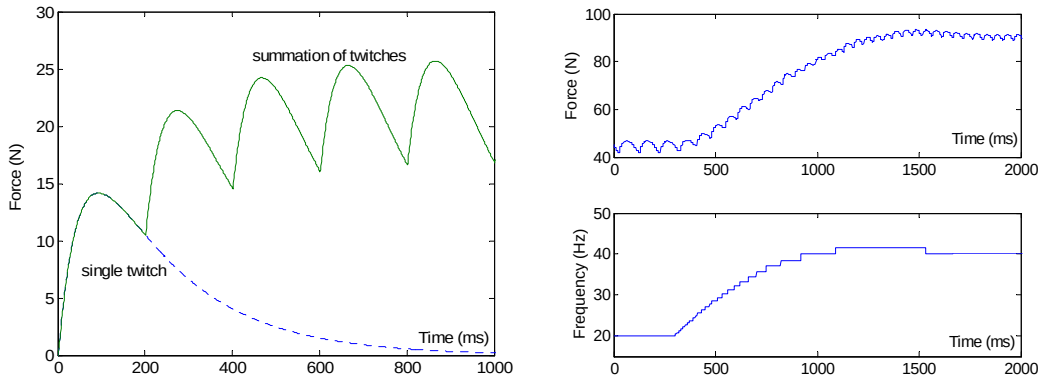

Fig. 2. Single Twitch (dotted) and Summation of Twitches (continuous) at 5Hz (unit) impulse frequency in open loop (left) and a closed loop response with a DIRAC-PI controller (right)

2.2. A DIRECT ADAPTIVE CONTROLLER: DIRAC

Controller design is based on using the auto-tuning principle, which automatically finds a set of PI(D) parameters without an *a priori* process identification (i.e. no model required). A brief description is provided in this section and more details can be found in [3].

The PI(D) parameters can further be used in a discrete-time control scheme, with a software implemented controller:

$$u(t) = u(t-1) + c_0 e(t) + c_1 e(t-1) + c_2 e(t-2) \tag{2}$$

with the error being the difference between the desired force w(t) and the measured force y(t):

$$e(t) = w(t) - y(t) \tag{3}$$

Denoting the shift-operator: $q^{-1}e(t) = e(t-1)$, results:

$$u(t) = \frac{C(q^1)}{1-q^{-1}} e(t) = \frac{c_0 + c_1 q^{-1} + c_2 q^{-2}}{1-q^{-1}} e(t) \tag{4}$$

and the control loop is depicted in Figure 1.

In [3] is mentioned that "*the DIRAC algorithm can be considered as an auto-tuning as well as an adaptation method*". Indeed, since the identification of the controller parameters is done within the DIRAC strategy, there is no need for *a priori* specifying a model of the process, thus functioning as an *auto-tuning* method. Secondly, if used *on-line*, the PI(D) parameters are adapted continuously, resulting thus in a direct *adaptive* controller. The use of auto-tuning or adaptive control seems appropriate for control of skeletal muscles, since they are known to be time-varying. The adaptive control method described in this section is easy to understand and simple to apply. In the context of an unknown process model, the assumption that the muscle and the stimulator are described by an unknown (discrete-time) transfer function $MS(q^{-1})$ leads to the closed loop transfer function:

$$y(t) = \frac{C(q^{-1})MS(q^{-1})}{(1-q^{-1}) + C(q^{-1})MS(q^{-1})} w(t) \tag{5}$$

The *design performance* of the closed loop is specified by a *reference model,* $R(q^{-1})$, given *a priori*. For example, one of the desired characteristics of the closed loop response can be the settling time. The task of controller tuning is to find $C(q^{-1})$ (i.e. c_0, c_1 and c_2) such that the closed-loop transfer function from (5) approximates the desired reference model $R(q^{-1})$. This can be written as:

$$C(q^{-1})(1-R(q^{-1}))MS(q^{-1}) \cong (1-q^{-1})R(q^{-1}) \tag{6}$$

Applying (6) to the time-signal $u(t)$, results in

$$C(q^{-1})(1-R(q^{-1}))\underbrace{MS(q^{-1})u(t)}_{y(t)} \cong (1-q^{-1})R(q^{-1})u(t) \tag{7}$$

and becomes:

$$C(q^{-1})(1-R(q^{-1}))y(t) \cong (1-q^{-1})R(q^{-1})u(t) \tag{8}$$

Defining the filtered signals:

$$u_f(t) = (1-q^{-1})R(q^{-1})u(t),\ y_f(t) = (1-R(q^{-1}))y(t) \tag{9}$$

and introducing the error signal $\varepsilon(t)$, (8) becomes:

$$\boxed{u_f(t) = C(q^{-1})y_f(t) + \varepsilon(t)} \tag{10}$$

The final step is to estimate (e.g. via least-squares estimator) the parameters in the polynomial $C(q^{-1})$ such that the errors $\varepsilon(t)$ are minimized. The overall scheme is presented in Figure 3.

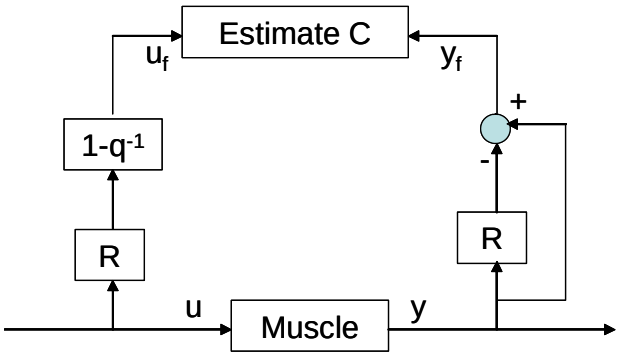

Fig. 3. Scheme of the DIRAC Strategy

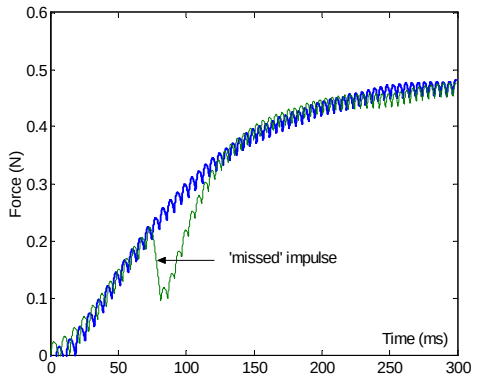

Fig. 4. Effect on results of the numerical errors in the stimulus function

Notice that for the simulation presented in this contribution, DIRAC algorithm has been used *off-line*, for initial tuning of a PI controller; nevertheless, the method can be easily implemented *on-line*, as a direct adaptive controller. The DIRAC-PI controller parameters applied in this case are: K_p=0.01 and T_i=0.01, with a sampling period of T_s=10 ms.

2.3. PERFORMANCE ANALYSIS

The experiment consisted in *changing the reference set-point* (= force) from 45N to 95N. On a scale of 22.5N-225N (corresponding to the nominal input range of 5Hz-50Hz), a set-point change of 50N is about 25%. The result given by the controller is depicted in Figure 2 along with its corresponding control input. Applying adaptive control techniques for skeletal muscle control is strongly motivated by the time-varying character of the system (i.e. in rehabilitation systems). In [10] it has been shown that a similar performance can be obtained with an adaptive control strategy as with a controller which is designed based on the model of the system. However, the obvious advantage is that DIRAC strategy does not require an *a priori* knowledge of the model, it can be easily used *on-line* (and implemented in discrete time) and tackles the problems imposed by time-varying systems.

An interesting challenge is posed by the software implementation of such a stimulus function, due to its discrete nature. If some conditions for numerical accuracy (timing) are not respected, the results are strongly influenced (Figure 4). More detailed description of this issue is given in [10].

3. APPLICATION II: GLUCOSE LEVEL CONTROL IN TYPE I DIABETIC PATIENTS

Diabetes Mellitus is an incurable disease affecting millions of people worldwide. Belgium is one of the leading countries in the astringent fight against the increasing number of diabetic patients so that this *contemporary disease* does not reach its current prediction of 50 million victims in Europe by 2025 [8]. In parallel, scientists are focusing on developing a manifold of new techniques and feasible instrumentation to offer wearable solutions and improve the life of type I diabetic patients. Type I, or insulin-dependent diabetes mellitus, is characterized by insufficient secretion of insulin from the pancreas, resulting in plasma glucose concentrations elevated beyond the *normoglycemic range* (65-120mg/dL).

The treatment methods for insulin-dependent diabetes, subcutaneous insulin injection or continuous infusion of insulin, usually result in frequent variations of glucose concentration in blood. Therefore, a significant effort has been put toward the development of a device to control glycemia [1, 7, 12] and the methods are continuously improved. A device of this type would contain three major components: i) a pump; ii) an in vivo glucose sensor; and iii) a processor with a mathematical algorithm to regulate the pump given a sensor measurement. Technological advances allowed a wide variety of programmable and variable-rate infusion pumps to become available.

An *in-house* predictive control algorithm (EPSAC) [4] has been implemented to control blood glucose level in type I diabetic patients, by controlling the insulin infusion rate of a pump. Comparison between the performance obtained with a linear model and a nonlinear model used in the prediction algorithm is discussed. Controller performance was assessed in terms of its ability to reject a meal disturbance (30g glucose) around the normoglycemic setpoint (81mg/dL) and around a glycemic point of no practical interest, but for academic purposes. Results from unconstrained control are presented, and the control strategy has discrete representation, being feasible for implementation in wearable embedded processor devices.

3.1. A GENERALIZED PATIENT MODEL

An injected glucose load in normal (glucose tolerant) individuals immediately elevates the glucose concentration in plasma. This initiates the secretion of insulin from the pancreatic ß-cells. The provoked hyperglycemia induces an immediate peak in the insulin concentration in plasma, and the glucose uptake in muscles, liver and adipose tissue is raised by the *remote insulin* in action. This lowers the glucose concentration in plasma, affecting the ß-cells to secrete less insulin (biological feedback). By 1 hour the glucose concentration is normalized and in the following 2 hours a moderate undershoot is observed. After 2-3 hours, it is usually found that the perturbed insulin and glucose concentrations have returned to normal. A simple yet reliable mathematical representation of glucose and insulin kinetics is necessary before implementing the EPSAC model-based control scheme. The *Bergman minimal model* was investigated [2]. A generalized (averaged) model has been derived based on the patient data from [2] and the values of the coefficients describing glucose kinetics are: p_1=-3.38*10^{-2} min^{-1} ; p_2=-2.09*10^{-2} min^{-1} ; p_3=7.512*10^{-6} min^{-2}/µU/ml, respectively, the values of the coefficients describing the insulin kinetics are: γ=2.756*10^{-3} µU/mg min^2 ; h=98.08 mg/dl; n=0.214 min^{-1}. These coefficients are used in the following differential equations:

$$\dot{G}(t) = (p_1 - X(t))G(t) + p_1 G_B + Dist(t), G(0) = G_0$$
$$\dot{X}(t) = p_2 X(t) + p_3 (I(t) - I_B(t)), X(0) = 0 \quad (12)$$
$$\dot{I}(t) = \gamma (G(t) - h)t - n(I(t) + I_B(t)) + U(t), I(0) = I_0$$

where:

p_1 – a constant rate for glucose uptake in muscles, liver and tissues;
p_3 is referred to as the insulin-dependent increase in glucose uptake ability in tissue;
p_2 – a constant denoting intra-cellular metabolism of the remote insulin effect;
I(t) – plasma insulin, fills a remote insulin compartment with a constant rate p_3;
X(t) - denotes the dynamic insulin response proportional to the active insulin in the remote compartment and describes the time dependent effect of the insulin on the net glucose disappearance;
G(t) - the plasma glucose concentration governed by the balance between the glucose production/uptake by the liver and the utilization of glucose by the peripheral tissues;
G_B and I_B - basal levels of glucose and insulin
n - the fractional disappearance of insulin
h - threshold level for ß-cells release
γ - the rate of ß-cells release
U(t) - the insulin infusion rate delivered by the pump.

A detailed description for the compartmental model and its parameters can be found in [2].

3.2. AN IN-HOUSE PREDICTIVE CONTROL: EPSAC

The EPSAC strategy [4] is based on a generic process model:

$$y(t) = x(t) + n(t) \quad (13)$$

The disturbance $n(t)$ includes the effects in the measured output $y(t)$ (in this case: glucose concentration *G(t)*) which do not come from the model input $u(t)$ (in this case: insulin infusion rate *U(t)*) via the available model. These non-measurable disturbances have a stochastic character with non-zero average value, which can be modelled by a coloured noise process:

$$n(t) = \left[C(q^{-1}) / D(q^{-1}) \right] \cdot e(t) \quad (14)$$

with: *e(t)* - uncorrelated (white) noise with zero mean value; $C(q^{-1})$ and $D(q^{-1})$ - monic polynomials in the backward shift operator q^{-1} of orders n_c and n_d. The filter $C(q^{-1})/D(q^{-1})$ is considered to be a *design filter* [5]. The model output $x(t)$ represents the effect of the control input $u(t)$ on the process output $y(t)$ and is also a non-measurable signal, and the relationship between $u(t)$ and $x(t)$ is given by the generic dynamic system model, which can be obtained from (12):

$$x(t) = f\left[x(t-1), x(t-2), \cdots, u(t-1), u(t-2), \cdots \right] \quad (15)$$

The fundamental step in MBPC methodology consists in prediction of the process output $y(t+k)$ at time instant *t*, indicated by $\{ y(t+k \mid t),\ k = 1 \ldots N_2 \}$, over the *prediction horizon* N_2, and based on:

– the measurements available at sampling time instant t: $\{y(t), y(t-1), \cdots, u(t-1), u(t-2), \cdots\}$;

– the future values of the input signal (postulated at time t): $\{u(t \mid t), u(t+1 \mid t), \cdots\}$.

Using the generic process model, the predicted values of the output are:

$$y(t+k \mid t) = x(t+k \mid t) + n(t+k \mid t) \tag{16}$$

Prediction of $x(t+k|t)$ and of $n(t+k|t)$ can be done respectively by recursion of the process model (13) and by using filtering techniques on the noise model (14).

The future response is considered as being the cumulative result of two effects:

$$y(t+k \mid t) = y_{\text{base}}(t+k \mid t) + y_{\text{optimize}}(t+k \mid t) \tag{17}$$

Refer to Figure 5 for the concepts of *base* and *optimizing* controls. Notice that $u(t+k|t)$ is constrained to be constant from $k=N_u$ on (and this is realized by *selecting* $u_{\text{base}}(t+k|t)$ constant from $k=N_u$ on and by *imposing* that $\delta u(t+k|t)$ should be constant from $k=N_u$ on). The *design* parameter N_u is called the *control horizon* (a well-known concept in Model Based Predictive Control literature).

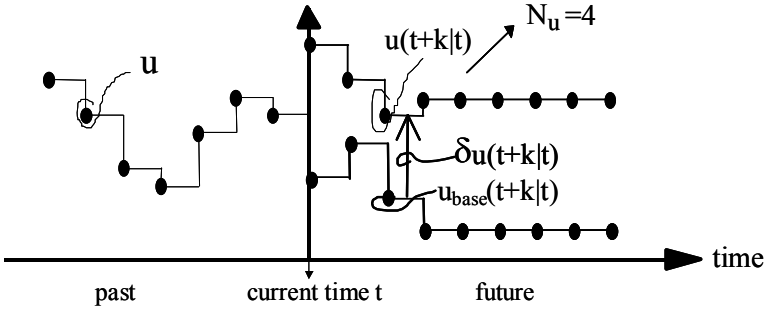

Fig. 5. The EPSAC concept of *base/optimizing* controls

Equation (17) is valid, however, for linear systems only (from the principle of superposition). For nonlinear systems, by selecting the base control strategy $u_{base}(t+k/t)$ appropriately, the term $y_{opt}(t+k/t)$ can be made zero in an iterative way. This will result in an optimal solution for nonlinear systems, without a preliminary linearization of the system. The nonlinear model is then used directly to calculate the base responses $y_{base}(t+k/t)$ at every iteration and also for calculating the required step and impulse response coefficients (G-matrix). The key EPSAC-MBPC equation is:

$$\mathbf{Y} = \bar{\mathbf{Y}} + \mathbf{G}\mathbf{U} \tag{18}$$

where (with $[...]^T$ denoting the matrix transpose):

$$\mathbf{Y} = \left[y(t+N_1 \mid t) \cdots y(t+N_2 \mid t) \right]^T \tag{19a}$$

$$\bar{\mathbf{Y}} = \left[y_{\text{base}}(t+N_1 \mid t) \cdots y_{\text{base}}(t+N_2 \mid t) \right]^T \tag{19b}$$

$$\mathbf{U} = \left[\delta u(t \mid t) \cdots \delta u(t + N_u - 1 \mid t)\right]^T \tag{19c}$$

$$\mathbf{G} = \begin{bmatrix} h_{N_1} & h_{N_1-1} & h_{N_1-2} & \cdots & g_{N_1-N_u+1} \\ h_{N_1+1} & h_{N_1} & h_{N_1-1} & \cdots & \cdots \\ \cdots & \cdots & \cdots & \cdots & \cdots \\ \cdots & \cdots & \cdots & \cdots & \cdots \\ h_{N_2} & h_{N_2-1} & h_{N_2-2} & \cdots & g_{N_2-N_u+1} \end{bmatrix} \tag{19d}$$

The controller output is then the result of minimizing the cost function:

$$V(\mathbf{U}) = \sum_{k=N_1}^{N_2} [r(t+k \mid t) - y(t+k \mid t)]^2 \tag{20}$$

with $r(t+k \mid t)$ the desired *reference trajectory* (desired glucose level) and the *horizons* N_1, N_2 being design parameters.

The cost function (20) is a quadratic form in **U,** having the following structure using the matrix notation from (19) and with **R** defined similarly to **Y** (but containing the $r(t+k \mid t)$ values):

$$V(\mathbf{U}) = [\mathbf{R} - \bar{\mathbf{Y}} - \mathbf{G}\mathbf{U}]^T [\mathbf{R} - \bar{\mathbf{Y}} - \mathbf{G}\mathbf{U}] \tag{21}$$

which leads after minimization w.r.t. **U** to the optimal solution:

$$\mathbf{U}^* = [\mathbf{G}^T\mathbf{G}]^{-1}\mathbf{G}^T(\mathbf{R} - \bar{\mathbf{Y}}) \tag{22}$$

The matrix $\mathbf{G}^T\mathbf{G}$ which has to be inverted has dimension N_u x N_u. For the default case N_u=1, this results in a simple *scalar* control law. Only the first element $\delta u(t/t)$ in $\mathbf{U}^*$ is required in order to compute the actual control input applied to the process:

$$u(t) = u_{\text{base}}(t \mid t) + \delta u(t \mid t) = u_{\text{base}}(t \mid t) + \mathbf{U}^*(1) \tag{23}$$

At the next sampling instant t+1, the whole procedure is repeated taking into account the new measurement information $y(t+1)$. This is called the principle of *receding horizon control*, another well-known MBPC-concept. A detailed description of the algorithm is given in [4] with some practical guidelines for implementation, extensions to constrained control and multi-input, multi-output case with examples.

3.3. LINEAR VERSUS NONLINEAR EPSAC PERFORMANCE

If insulin is applied in excess, the blood glucose level goes below normal (<65mg/dL) causing *hypoglycemia*. *On a short term*, hypoglycemia can induce fainting, muscle convulsions, deeper state of consciousness-loss such as coma. On the other hand, if insulin is supplied insufficiently, the blood glucose level elevates above the normoglycemia values (>120mg/dL) causing the condition known as *hyperglycemia*. It is thought that most of *the long-term complications* associated with diabetes, such as nephropathy (any kidney disease) and retinopathy (diseased condition of the eye-

retina, esp. non-inflammatory) result from *sustained* hyperglycemia [11], thus an immediate return to the normoglycemic values is important.

As mentioned before in the beginning of this section, the effect of infusing (exogenous) glucose is examined and controllers (linear-LEPSAC, nonlinear-NEPSAC) are compared. Notice that the insulin infusion rate is also constrained between 0-100 mU/ml (it cannot go negative because it cannot be taken out of patient's body). It is expected that the nonlinear model used with NEPSAC leads to improved results compared to the linearized model used in LEPSAC. A bolus (e.g. meal) of 30g glucose is considered as the input disturbance to the closed loop system. In the first case, the reference is considered within the normoglycemic range: 81mg/dL and the output result (glucose level) along with its corresponding control effort (insulin injection rate) are depicted in Figure 6-left.

$$P_{81}(s) = \frac{-0.0006}{s^3 + 0.3609s^2 + 0.01911s + 0.000256} \tag{24}$$

$$P_{50}(s) = \frac{-0.0003756}{s^3 + 0.3609s^2 + 0.01911s + 0.000256} \tag{25}$$

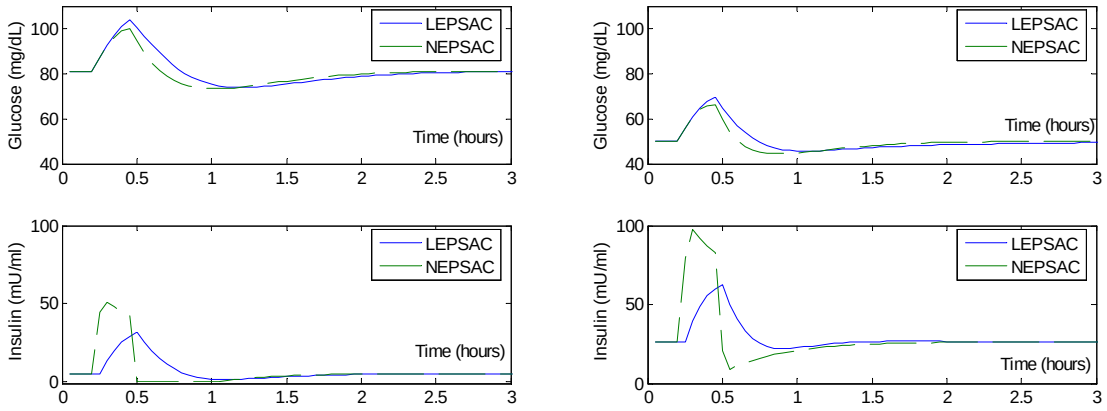

Fig. 6. Disturbance rejection around the normoglycemic point of 81.1mg/dL (left) and 50mg/dL (right)

Looking at Figure 6-left, can be observed that the linear EPSAC (based on a linearized model around the 81.1mg/dL point on the static characteristic of the system – equation 24) gives similar performance as the nonlinear EPSAC (based on the direct use of the nonlinear model of the patient). This observation is however based on a comparison between the two controllers which is not realistic: the command for the nonlinear EPSAC between 0.5–1hour is zero and the system can be considered in open loop! Therefore, in order to make a real performance comparison, the system must be tested in an operating point where the control effort is not enter the constrained area (here we are not using constrained EPSAC algorithm; the constraints are imposed after the calculation of the optimal command). The point of 50mg/dL has been considered as the novel operating point and the results are given in Figure 6-right (LEPSAC uses the corresponding linearized model – equation 25). Notice that the control design parameters are always the same for both situations and both linear and nonlinear EPSAC algorithm: N_u=1, N_1=1,N_2=20, with a sampling period of 3 minutes.

4. DISCUSSION

The use of adaptive autotuning control strategies such as DIRAC in closed-loop control of paralyzed skeletal muscles is strongly justified by the inter- and intra- patient variability. The muscle properties differ from person to person (e.g. age, weight, fit) as well as from one time-interval to another (e.g. in recovery, rehabilitation systems). In [10] has been shown that comparable results can be obtained without knowledge of a muscle-model (thus no need for a preliminary identification of the muscle!). This means that a wearable device can be supported, applied and used successfully on any patient, due to the auto-tuning, adaptive character of the DIRAC control strategy. Taking into account the time delay present in the system is important for real life applications, and satisfactory and stable results are obtained.

Regarding the second example, using predictive control gives a possibility to estimate the future glucose behaviour based on the past insulin inputs. The measurement of the patient's actual glucose level is used as feedback signal to correct the glucose concentration predictions (based on the patient model). By definition, the predictive controller takes action for a *predicted* hypo- or hyperglycemic state of the patient before it occurs. Moreover, if used in constrained control, the predictive algorithms provide optimal results in coping with the imposed constraints on input-output variables. However, in the present contribution has not been applied constrained control to EPSAC, but the design of the N_u, N_1 and N_2 parameters had been made such that it copes reasonably well within the imposed constraints (limits are applied after calculation of the controller output).

An interesting application of the EPSAC algorithm to blood glucose control in type I diabetic patients has been provided, with a practical interpretation of the control problem. Constrained control and robustness tests within the normoglycemic range are the subject of ongoing research with possibilities for implementation in a wearable device. The example for second linearization point (50mg/dL) has no relevance in practice, but it is used to compare the performance of the two controllers, whereas the control action lies within the constrained zone (0-100mU/ml insulin infusion rate).

In the context of real-life implementation, a common advantage of the DIRAC-PI and EPSAC-MBPC strategies stand in their discrete nature, making them feasible for implementation in nowadays DSP (digital signal processing) circuit technology.

5. CONCLUSIONS

The present contribution has given a brief overview upon the practical problems posed to a control engineer. The task of developing stable and robust control algorithms does not limit to a simple mathematical description. Real-life constraints and hardware/software limitations are to be tackled in an optimal manner, providing a feasible, practical oriented solution.

Although a more advanced control can be applied to these 2 examples (i.e. constrained nonlinear predictive control), the aim of this presentation has been limited to a simple but satisfactory solution. Performance is discussed from practical implementation requirements, as well as from an academic point of view. A more technical description of the implemented algorithms is provided by use of referenced publications.

Robustness tests make the objective of an on-going research for both applications, with the long-term aim to be implemented in a real-life wearable device.

BIBLIOGRAPHY

[1] BELAZZI R., NUCCI G., COBELLI C., The subcutaneous route to insulin-dependent diabetes therapy, *IEEE Engineering in Medicine and Biology,* Vol. 20, No. 1 pp. 54-64, 2001.

[2] BERGMAN R., PHILLIPS S., COBELLI C., Physiologic evaluation of factors controlling glucose tolerance in man, J. Clin. Invest. Vol. 68, No. 12, pp. 1456-1467, 1981

[3] DE KEYSER R., DIRAC: A Direct Adaptive Controller, IFAC Workshop on Digital Control: Past, Present and Future of PID Control, Spain, 2000, 199-204

[4] DE KEYSER R., Model Based Predictive Control for Linear Systems, *UNESCO Encyclopaedia of Life Support Systems,* Article contribution 6.43.16.1, Eolss Publishers Co Ltd, Oxford, ISBN 0 9542 989 18-26-34 (www.eolss.net), 30p., 2003.

[5] DE KEYSER R., IONESCU C., The disturbance model in model based predictive control, Proc. *IEEE Conf. on Control Applications,* Istanbul, Turkey, June 2003, paper id 001472.

[6] DEVASAHAYAM S.R., Signals and Systems in Biomedical Engineering, Modelling Skeletal Muscle Contraction (Kluwer Academics, Ed: E.M. Tzanakou) pp. 235-266, 2000

[7] FISHER E.M., A semi-closed loop algorithm for the control of blood glucose levels in diabetics, *IEEE Trans. on Biomedical Engineering,* Vol. 38, No. 1, pp.57-61, 1991.

[8] IDF-International Diabetes Federation, Annual Report 2004, 5p. Available:http://www.idf.org

[9] IEEE Control Engineering Series: Biological Systems, modelling and control, Ed.: D.A. Linkens, Alden Press Oxford, ISBN: 0-906048-15-X, 1979

[10] IONESCU C., DE KEYSER R., Adaptive closed-loop control strategy for paralyzed skeletal muscles, Proc. of the IASTED Int. Conf. on Biomedical Engineering, Innsbruck, Austria, February 2005, pp. 667-672

[11] GUYTON A.C., Textbook of Medical Physiology. 7th Edition. Philadelphia, USA: Saunders W.B., 1986

[12] PARKER R.S., DOYLE III F.J., PEPPAS N.A., A model based algorithm for blood glucose control in type I diabetic patients, *IEEE Trans. on Biomedical Engineering,* Vol. 46, No. 2, pp.148-157, 1999

[13] Proc. of the IFAC Int. Conf. on Regulation and control in Physiological Systems, August 1973, Rochester NY, USA

[14] RICHMOND F., LOEB G.E., DUPONT A.C., BAGG S.D., CREASY J.L., ROMANO C., ROMANO D., Clinical trials of BIONs for therapeutic electrical stimulation, Proc. 23rd Annual Conf. of the IEEE Eng. in medicine and biology Soc, Istanbul, Turkey, 4p, 2001